DO NOT ENTER: /S.J./

RESPONSE UNDER 37 CFR § 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1617

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 7940**
Yukiko YOKOI et al.	:	Attorney Docket No. 2005_0520A
Serial No. 10/530,046	:	Group Art Unit 1617
Filed April 1, 2005	:	Examiner Samira JM Jean-Louis
ANTIBIOTIC PHARMACEUTICAL COMPOSITION WITH IMPROVED ORAL ABSORBABILITY	:	**Mail Stop: AF**

AMENDMENT AFTER FINAL REJECTION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

Sir:

Responsive to the final Office Action of November 17, 2008, the time for responding thereto being extended for one month in accordance with a fee for Extension of Time submitted herewith, please amend the above-identified application as follows:

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A pharmaceutical composition comprising amorphous cefditoren pivoxil and a sucrose ~~ester~~ fatty acid ester, which is obtainable by mixing or wet-granulating particles containing amorphous cefditoren pivoxil with the sucrose ~~ester~~ fatty acid ester while amorphous cefditoren pivoxil maintains its particle state, wherein crystallization of the amorphous cefditoren pivoxil is inhibited.

2. (Currently amended) The pharmaceutical composition according to claim 1, wherein the weight ratio of the sucrose fatty acid ester to the cefditoren pivoxil is in a range of from 0.0008 to 0.816 ~~which contains 0.1 to 100 mg of the sucrose ester fatty acid on the basis of an amount equivalent to 100 mg efficacy of cefditoren pivoxil~~.

3. (Previously presented) The pharmaceutical composition according to claim 1, which further comprises a pharmaceutically acceptable polymer.

4. (Previously presented) The pharmaceutical composition according to claim 3, wherein the polymer is one or more water-soluble high polymers selected from the group consisting of hydroxypropylmethyl cellulose, methylcellulose, hydroxyethyl cellulose, polyvinylpyrrolidone, and hydroxypropyl cellulose.

5. (Currently amended) The pharmaceutical composition according to claim 3, wherein the weight ratio of the polymer to the cefditoren pivoxil is in a range of from 0.008 to 0.816~~which contains 1 to 100 mg of the polymer on the basis of an amount equivalent to 100 mg efficacy of cefditoren pivoxil~~.

6. (Previously presented) The pharmaceutical composition according to claim 1, which further comprises one or more pharmaceutically acceptable additives.

7. (Previously presented) The pharmaceutical composition according to claim 2, which further comprises a pharmaceutically acceptable polymer.

8. (Previously presented) The pharmaceutical composition according to claim 7, wherein the polymer is one or more water-soluble high polymers selected from the group consisting of hydroxypropylmethyl cellulose, methylcellulose, hydroxyethyl cellulose, polyvinylpyrrolidone, and hydroxypropyl cellulose.

9. (Currently amended) The pharmaceutical composition according to claim 4, wherein the weight ratio of the polymer to the cefditoren pivoxil is in a range of from 0.008 to 0.816~~which contains 1 to 100 mg of the polymer on the basis of an amount equivalent to 100 mg efficacy of cefditoren pivoxil~~.

10. (Currently amended) The pharmaceutical composition according to claim 7, wherein the weight ratio of the polymer to the cefditoren pivoxil is in a range of from 0.008 to 0.816~~which contains 1 to 100 mg of the polymer on the basis of an amount equivalent to 100 mg efficacy of cefditoren pivoxil~~.

11. (Currently amended) The pharmaceutical composition according to claim 8, wherein the weight ratio of the polymer to the cefditoren pivoxil is in a range of from 0.008 to 0.816~~which contains 1 to 100 mg of the polymer on the basis of an amount equivalent to 100 mg efficacy of cefditoren pivoxil~~.

12. (Previously presented) The pharmaceutical composition according to claim 2, which further comprises one or more pharmaceutically acceptable additives.

13. (Previously presented) The pharmaceutical composition according to claim 3, which further comprises one or more pharmaceutically acceptable additives.

14. (Previously presented) The pharmaceutical composition according to claim 4,

which further comprises one or more pharmaceutically acceptable additives.

15. (Previously presented) The pharmaceutical composition according to claim 7, which further comprises one or more pharmaceutically acceptable additives.

16. (Previously presented) The pharmaceutical composition according to claim 8, which further comprises one or more pharmaceutically acceptable additives.

17. (Previously presented) The pharmaceutical composition according to claim 9, which further comprises one or more pharmaceutically acceptable additives.

18. (Previously presented) The pharmaceutical composition according to claim 10, which further comprises one or more pharmaceutically acceptable additives.

19. (Previously presented) The pharmaceutical composition according to claim 11, which further comprises one or more pharmaceutically acceptable additives.

20. (Currently amended) A pharmaceutical composition comprising particles having amorphous cefditoren pivoxil present in an interior portion of said particles and a sucrose ~~ester~~ fatty acid ester present in an exterior portion of said particles, wherein crystallization of amorphous cefditoren pivoxil is inhibited.

21. (Currently amended) The pharmaceutical composition of claim 20, wherein the sucrose ~~ester~~ fatty acid ester has a hydrophilic to lipophilic balance (HLB) value greater than 10.

22. (Currently amended) The pharmaceutical composition of claim 20, wherein said sucrose ~~ester~~ fatty acid ester has an HLB value in a range of from 11 to 20.

23. (Previously presented) The pharmaceutical composition of claim 20, further comprising a pharmaceutically acceptable polymer.

24. (Previously presented) The pharmaceutical composition of claim 23, wherein said pharmaceutically acceptable polymer includes at least one polymer selected from the group consisting of hydroxypropylmethyl cellulose, methyl cellulose, hydroxyethyl cellulose, polyvinylpyrrolidone, and hydroxypropyl cellulose.

25. (Previously presented) The pharmaceutical composition according to claim 20, in a dose form containing from about 300 to 800 milligrams of amorphous cefditoren pivoxil.

26. (Previously presented) The pharmaceutical composition of claim 20 in a tableted dose form.

27-30. (Cancelled)

31. (Currently amended) The pharmaceutical composition according to claim 1, wherein the sucrose ~~ester~~ fatty acid ester has an HLB value of 11 to 20.

32. (Previously presented) The pharmaceutical composition according to claim 1, wherein the composition is free from polysorbate 80.

33. (Previously presented) The pharmaceutical composition according to claim 1, which has an amorphousness-retaining character of the amorphous cefditoren pivoxil in aqueous medium of at least one day.

34. (Previously presented) The pharmaceutical composition according to claim 1, which has an amorphousness-retaining character of the amorphous cefditoren pivoxil in aqueous medium of at least two days.

35. (Currently amended) The pharmaceutical composition according to claim 20, wherein the sucrose ~~ester~~ fatty acid ester has an HLB value of 11 to 20.

36. (Previously presented) The pharmaceutical composition according to claim 20, wherein the composition is free from polysorbate 80.

37. (Previously presented) The pharmaceutical composition according to claim 20, which has an amorphousness-retaining character of the amorphous cefditoren pivoxil in aqueous medium of at least one day.

38. (Previously presented) The pharmaceutical composition according to claim 20, which has an amorphousness-retaining character of the amorphous cefditoren pivoxil in aqueous medium of at least two days.

39. (New) A pharmaceutical composition comprising amorphous cefditoren pivoxil and sucrose fatty acid ester, wherein the weight ratio of the sucrose fatty acid ester to the amorphous cefditoren pivoxil is in a range of from 0.0008 to 0.04, and wherein the composition is capable of retaining the amorphicity of said amorphous cefditoren pivoxil in aqueous medium for at least one day.

40. (New) A pharmaceutical composition comprising amorphous cefditoren pivoxil in combination with an amount of sucrose fatty acid ester that is effective to maintain said amorphous cefditoren pivoxil in an amorphous state in aqueous medium for a period of at least one day.

REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Consideration After Final Rejection

Although this amendment is presented after final rejection, the Examiner is respectfully requested to enter the amendments and consider the remarks, as they clarify prior mistranslations, address the indefiniteness rejection, and place the application in condition for allowance.

Summary of Telephone Discussions with Examiner

Applicants wish to kindly thank the Examiner for her time and helpful comments during the telephone discussions of December 1, 2008 and January 30, 2009.

During the discussions, Applicants indicated that they would be filing a verified English translation of the international application, indicating that "sugar ester fatty acid" was a mistranslation in the original English translation, and that "sucrose fatty acid ester" is a better translation. The Examiner indicated that this would be acceptable to overcome her concerns.

Additionally, Applicants discussed that the Japanese term "ri-ki-ka" in the original international application could be translated as "efficacy", but is better translated as "potency". The Examiner indicated that a verified English translation indicating such should be helpful in addressing the indefiniteness rejection.

Additionally, the Examiner indicated that it is not necessary to file a verified English translation of the priority document at this time. However, the Examiner noted that if an "intervening" reference (i.e., a reference with an effective date between the priority date and the international filing date) is applied, then it may be necessary to file a verified English translation of the priority document at that time.

True (and Verified) English Translation of International (PCT) Application

As mentioned above, a true verified English translation of the international application is submitted herewith.

Amendments to the Specification and Claims

In view of the verified English translation of the international application submitted herewith, Applicants have amended the specification to recite "potency" rather than --efficacy--, and have amended the specification and claims to recite "sucrose fatty acid ester" rather than --sucrose ester fatty acid--. (The specification was previously amended to change "sugar ester fatty acid" to --sucrose ester fatty acid--. However, the phrase "sucrose fatty acid ester" is more accurate.)

Claim 2 has been amended to recite that the weight ratio of the sucrose fatty acid ester to the cefditoren pivoxil is in a range of 0.0008 to 0.816. Claims 5 and 9-11 have been amended to recite that the weight ratio of the polymer to the cefditoren pivoxil is in a range of 0.008 to 0.816. Support for these amendments is found in the original claim language, in view of the discussion set forth below regarding the rejection under 35 U.S.C. § 112, second paragraph. Specifically, the Japanese Pharmacopoeia indicates that the potency of cefditoren pivoxil is expressed as mass (potency) of cefditoren, and that an amount equivalent to 100 mg potency of cefditoren pivoxil means 122.53 mg of cefditoren pivoxil. Thus, the weight ratios recited in claims 2, 5 and 9-11 are easily calculated. [0.1 mg sucrose fatty acid ester / 122.53 mg cefditoren pivoxil = 0.0008; 100 mg sucrose fatty acid ester / 122.53 mg cefditoren pivoxil = 0.816.]

Accordingly, although the amendments to claims 2, 5 and 9-11 are not expressly set forth in the specification, as stated by MPEP 2163.02, "the subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement."

Claims 1 and 20 have also been amended to recite that "crystallization of the amorphous cefditoren pivoxil is inhibited", in accordance with the Examiner's suggestion. Support for this limitation is found in the examples of Applicants' specification, such as page 11, lines 14-17 of Applicants' substitute specification filed herewith.

New claims 39 and 40 have also been added to the application. Support for new claim 39 is found on page 7, lines 6-9 and Tables 1 and 2 on pages 10 and 11 of Applicants' substitute specification (filed herewith). These passages indicate that the sucrose fatty acid ester can be 0.1 to 5 mg on the basis of an amount equivalent to 100 mg potency of cefditoren pivoxil. The

weight ratio of new claim 39 is easily calculated from this description. [0.1 mg / 122.53 mg = 0.0008; 5 mg / 122.53 mg = 0.04.]

Support for new claim 40 is found on page 4, lines 20-33, page 5 lines 11-15 and Tables 1 and 2 on pages 10 and 11 of Applicants' substitute specification (filed herewith).

No new matter has been added to the application by these amendments.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 2, 5 and 9-11 as being indefinite under 35 U.S.C. § 112, second paragraph is respectfully traversed.

The Examiner has taken the position that efficacy is a relative term, and states that it is unclear from the specification as to which effect of the drug the 100 mg efficacy pertains. However, as discussed above, the verified English translation of the international application indicates that "potency" is a better translation of the Japanese term than "efficacy". Accordingly, Applicants' specification has been amended to recite "potency".

Relevant pages of the Japanese Pharmacopoeia Fifteenth Edition (English version) were submitted with Applicants' previous response, indicating that the potency of cefditoren pivoxil ($C_{25}H_{28}N_6O_7S_3$; M.W. 620.72) is expressed as mass (potency) of cefditoren ($C_{19}H_{18}N_6O_5S_3$; M.W. 506.58). This indicates that an amount equivalent to 100 mg potency of cefditoren pivoxil means 122.53 mg of cefditoren pivoxil.

Applicants have shown that "potency" is understood by those skilled in the art as a unit used for expressing an amount of an active moiety of an antibiotic.

The Examiner indicates that the Japanese Pharmacopoeia Fifteenth Edition (submitted with Applicants' previous response) clearly indicates that the potency of cefditoren pivoxil can be expressed as mass of cefditoren. However, the Examiner states that the document does not show that efficacy is synonymous with potency. This position is moot in view of the amendments to Applicants' claims and specification.

Additionally, the Examiner states that "in the pharmacology art . . . potency is a measure of the concentrations of a drug at which it is effective". Thus, the Examiner recognizes that "potency" is a term which is clearly understood by those of ordinary skill in the art.

Further, as discussed above, Applicants have amended claims 2, 5 and 9-11 to set forth

weight ratios of sucrose fatty acid ester or polymer to cefditoren pivoxil, based upon the teachings of the specification and the knowledge in the art (as evidenced by the Japanese Pharmacopoeia). Applicants have amended the claims in this manner because the term "weight ratio" is readily understood by those of ordinary skill in the art.

Thus, based upon MPEP 2173.02, which explains that the definiteness of claim language must be analyzed, not in a vacuum, but in light of the specification, the teachings of the prior art and the interpretation which would be given to the claim by one of ordinary skill in the art, Applicants' claims 2, 5 and 9-11 are not indefinite.

Therefore, Applicants respectfully assert that the above rejection should accordingly be withdrawn.

The Examiner also indicates that Applicants' claim of adding 0.1 to 100 mg of a sucrose fatty acid ester on the basis of an amount equivalent to 100 mg efficacy is indefinite as addition of any dosage of a non-active to obtain an amount equivalent to 100 mg efficacy of an active is highly unlikely. This is not a proper basis for a rejection under 35 U.S.C. 112, second paragraph, and thus, Applicants respectfully request that the Examiner withdraw this statement.

Patentability Arguments

The patentability of the present invention over the disclosures of the references relied upon by the Examiner in rejecting the claim will be apparent upon consideration of the following remarks.

Rejection Under 35 U.S.C. § 103(a)

The rejection of claims 1-26 and 31-38 under 35 U.S.C. § 103(a) as being unpatentable over Shimizu et al. (WO 00/06126) and Onodera et al. (U.S. Patent No. 6,486,149), and further in view of Hoffmann et al. (U.S. Patent Application Publication No. 2002/0015730) is respectfully traversed.

The Position of the Examiner

The position of the Examiner is of record. In response to Applicants' previous arguments, the Examiner takes the position that Applicants' contention that the Examiner has erroneously interpreted Shimizu, as Applicants' claims are directed to cefditoren pivoxil and a sucrose ester fatty acid and not a sugar ester fatty acid, is acknowledged but is not found persuasive. The Examiner states that the claims as previously presented recited the limitation of a pharmaceutical composition comprising amorphous cefditoren pivoxil and a sugar ester fatty acid. Accordingly, the Examiner has maintained this rejection on the ground that Applicants claims do not recite "sucrose ester fatty acid". In other words, the Examiner considers that the claims are still directed to "sugar ester fatty acid".

Applicants' Arguments

Applicants respectfully disagree with the Examiner's position for the following reasons.

As verified by the English translation of the international application submitted herewith, the recited term "sucrose fatty acid ester" is clearly supported. Accordingly, the Examiner is respectfully requested to carefully consider the arguments set forth in the previous response. Portions of these previously asserted arguments are set forth below for the Examiner's convenience.

Applicants' independent claim 1 requires a pharmaceutical composition comprising amorphous cefditoren pivoxil and a sucrose fatty acid ester. Applicants' independent claim 20 requires a pharmaceutical composition comprising particles, having amorphous cefditoren pivoxil in an interior portion of the particles, and sucrose fatty acid ester present in an exterior portion of the particles. Both independent claims have been amended to recite that crystallization of the amorphous cefditoren pivoxil is inhibited.

Shimizu et al. disclose a solid preparation comprising (i) a pharmacologically active ingredient, (ii) a sugar and (iii) a low-substituted hydroxypropyl cellulose. (Please see the abstract and claims of the reference.) The reference mentions sucrose fatty acid ester as a possible lubricant for the composition, on page 13, line 25. [Please disregard Applicants' argument in the prior response that this component, i.e., sucrose fatty acid ester, is not present in the Shimizu et al. reference.]

From a five page laundry list of acceptable active agents, the Examiner has pointed to cefditoren pivoxil. Similarly, from a three page laundry list of pharmaceutical additives, the Examiner has pointed to sucrose fatty acid ester. However, the Examiner has provided no motivation why one of ordinary skill in the art would select these two components from the broad teachings of the reference, to arrive at Applicants' invention.

Since there are no examples corresponding to the composition proposed by the Examiner, it appears that the Examiner is attempting to employ an "obvious to try" rationale, i.e., to try a formulation comprising two particular components, selected from two very large genera. However, Applicants respectfully assert that the "attempted" rationale employed by the Examiner in rejecting Applicants' claims was addressed by the Supreme Court in KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727 (U.S. 2007). The Examiner's rejection does not articulate the requirements necessary to reject the claims based on this rationale.

Discussion of the KSR Decision

In KSR, the Supreme Court addressed the "obvious to try" rationale, which has often been rejected by the Court of Appeals for the Federal Circuit. The Supreme Court did not indicate that "obvious to try" is always an appropriate rationale for proving obviousness. On the contrary, the Court stated, "[w]hen there is a design need or market pressure to solve a problem and there are a **finite** number of **identified**, **predictable** solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp . . . In that instance, the fact that a combination was obvious to try might show that it was obvious under § 103." See KSR, at 1742. (Emphasis added.)

Additionally, the USPTO issued Examination Guidelines for Determining Obviousness Under 35 § U.S.C. 103 in View of the Supreme Court Decision in KSR International Co. v. Teleflex Inc. These guidelines discuss the "obvious to try" rationale, stating that in order for an Examiner to reject a claim based on this rationale, the following must be articulated:

1) A finding that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market pressure to solve a problem;

2) A finding that there had been a finite number of identified, **predictable** potential solutions to the recognized need or problem;
3) A finding that one of ordinary skill in the art could have pursued the known potential solutions with a **reasonable expectation of success**; and
4) Whatever additional findings based on the *Graham* factors may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.

Relevance of the KSR Decision to Current Application

As discussed above, Shimizu et al. teach **many active agents** (spanning pages 4-9 of the reference), as well as **many pharmaceutical additives** (spanning pages 12-25 of the reference.) There is no criticality placed on the particular active agent, or on the pharmaceutical additive to be employed, as the disclosure is broad and generic. On the contrary, Applicants have identified a particular need, involving a particular active agent, i.e., cefditoren.

As discussed on page 4 of Applicants' substitute specification (filed herewith), a suspension in which crystals of cefditoren pivoxil were sufficiently suspended exhibited extremely low oral absorbability in dogs, as compared to an amorphous suspension. However, amorphous cefditoren pivoxil is apt to change into a crystalline state in a solution. Accordingly, an antibiotic pharmaceutical composition comprising amorphous cefditoren pivoxil is desired. (Please see page 4, lines 9-19 of the substitute specification filed herewith.)

As also discussed on page 4 of the substitute specification, Applicants have now found that crystallization of amorphous cefditoren pivoxil may be inhibited by simply mixing amorphous cefditoren pivoxil with sucrose fatty acid ester, and that a solid composition comprising a physical mixture of amorphous cefditoren pivoxil and a sucrose fatty acid ester was excellent in absorbability and immediate effect. Applicants indicate that this finding was surprising (i.e., unexpected) because, upon formulating amorphousized drugs into pharmaceutical preparations, a pharmaceutical preparation obtained by simply mixing active ingredients was known to be insufficient for its absorbability and immediate effect as compared to a solid dispersion compound or a soluble complex with cyclodextrin or the like. (Please see page 4, lines 20-33 of the substitute specification filed herewith.)

The Shimizu et al. reference discusses many active agents and additives, including

cefditoren pivoxil and sucrose fatty acid ester, but the reference makes no distinction among the laundry lists of components. Specifically, the reference fails to acknowledge the particular issues which are applicable to a composition comprising cefditoren pivoxil, as discussed in detail above.

There are many different active agents and additives in the world, each of which, in view of their chemical natures, possess distinct characteristics. As discussed above regarding KSR, the Supreme Court has indicated that the "obvious to try" rationale is appropriate only where there is a finite number of identified, **predictable** solutions with a **reasonable expectation of success**. Applicants respectfully assert that the Examiner has failed to satisfy this burden for two reasons. First, given the very large number of active agents and pharmaceutical additives discussed by the reference**,** it cannot be said that each and every combination of components from the reference would be predictable. Second, as discussed above, one of ordinary skill in the art would have been surprised by the results achieved by Applicants. Thus, there would be no reasonable expectation of success, based on the teachings of the reference.

Accordingly, under the Supreme Court's discussion regarding the "obvious to try" rationale, the Examiner's position is untenable and should be withdrawn.

Inappropriate Hindsight Rationale

Additionally, Applicants respectfully submit that one of ordinary skill in the art would not have chosen cefditoren pivoxil and sucrose fatty acid ester from the broad teachings of the cited reference, without the benefit of Applicants' disclosure. As also stated by the Supreme Court in KSR, "the factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." (See KSR, referring to Graham v. John Deere Co. of Kansas City, 86 S. Ct. 684, which warned against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to "guard against slipping into the use of hindsight". Accordingly, the Examiner's rejection is untenable on this basis as well.

Reference Fails to Teach Applicants' Unexpected Advantages

Additionally, the cited reference neither teaches nor suggests the advantages achieved by Applicants' claimed composition, and required by Applicants' amended claims. As described on page 4, lines 20 to 23 of the substitute specification filed herewith, Applicants discovered that crystallization of amorphous cefditoren pivoxil was inhibited by simply mixing amorphous cefditoren pivoxil with a sucrose fatty acid ester.

Further, Applicants' specification provides working examples showing the advantages of the addition of sucrose fatty acid ester in place of polysorbate 80 (which is employed by the Shimizu et al. reference). Specifically, the compositions of Examples 1 to 5 in Table 1 include amorphous cefditoren pivoxil and sucrose fatty acid ester while the composition of Reference Example 2 in Table 1 is a comparative composition containing polysorbate 80 in place of sucrose fatty acid ester. These compositions were tested in accordance with the procedure of Test Example 1.

As shown in Table 2, Reference Example 2 containing polysorbate 80 was immediately converted to a crystalline form while Examples 1 to 5 containing sucrose fatty acid ester with amorphous cefditoren pivoxil exhibited the amorphousness-retaining character of amorphous cefditoren pivoxil for at least two days. These results indicate that the claimed pharmaceutical compositions containing amorphous cefditoren pivoxil and sucrose fatty acid ester achieve high oral absorbability.

For the reasons discussed above, one of ordinary skill in the art would not have been motivated to form Applicants' claimed pharmaceutical composition, based on the teachings of Shimizu et al., nor would one of ordinary skill in the art have expected the advantages achieved by Applicants' composition, and required by Applicants' claims. Furthermore, neither of the secondary references remedies the deficiencies of Shimizu et al. in this regard.

Secondary References Do Not Remedy Deficiencies of Primary Reference

Additionally, as admitted by the Examiner, Shimizu et al. fail to teach or suggest "amorphous" cefditoren pivoxil. Although Onodera et al. disclose amorphous cefditoren pivoxil, the reference fails to remedy the deficiencies of Shimizu et al., and fails to teach or suggest the problem to be solved in the present application.

In fact, none of the cited references teach or suggest the problem to be solved by the present application. Specifically, as stated on page 4, lines 9 to 33 of Applicants' specification, the problem to be solved in the present application is to prevent amorphous cefditoren pivoxil from changing into a crystalline state in a solution, thereby improving the oral absorbability. However, none of the cited references even mention that amorphous cefditoren pivoxil is apt to change into a crystalline state in a solution, or that such a change adversely affects the oral absorbability. Accordingly, the cited references fail to recognize the problem discussed in Applicants' invention, and therefore do not teach or suggest a solution to said problem.

Claims Require that Crystallization of Amorphous Cefditoren Pivoxil Is Inhibited

In her response to Applicants' previous arguments, the Examiner indicated that Applicants' arguments with respect to the examples in the original specification which showed improved amorphous maintenance period of time of the claimed invention have been considered but are not found persuasive. The Examiner states that Applicants' arguments are directed to the newly added claims. This position of the Examiner is rendered moot by submission of the verified translation.

Additionally, the Examiner states that the features upon which Applicants rely (i.e., composition with an amorphousness-retaining character) are not recited in the rejected claims. Although Applicants do not acquiesce to the position that the unexpected results need be recited in the claims, in order to expedite allowance of the application, Applicants have amended the claims to recite that crystallization of the amorphous cefditoren pivoxil is inhibited. Accordingly, this position of the Examiner is also rendered moot.

Arguments Regarding Independent Claim 20

Regarding Applicants' claim 20, the Examiner states that Shimizu et al. teach the use of a third coating (i.e., enteric coating) containing a sugar fatty acid ester. Thus, the Examiner asserts that the active pharmacological ingredient is in the interior portion of the particles. However, as mentioned above, Applicants' claim 20 requires amorphous cefditoren pivoxil in an interior portion of the particles, and sucrose fatty acid ester present in an exterior portion of the particles. An enteric coating comprising a sugar fatty acid ester is clearly distinct from sucrose fatty acid

ester present in an exterior portion of particles. Thus, it is clear that claim 20, and the claims dependent thereon, are clearly patentable over the Shimizu et al. reference, taken alone, or in combination with the secondary references.

For the reasons set forth above, the subject matter of Applicants' claims is clearly patentable over the cited combination of references. Accordingly, the rejection should be withdrawn.

Arguments Regarding New Independent Claims 39 and 40

The pharmaceutical compositions recited in new claims 39 and 40 are patentable over Shimizu et al., since Shimizu et al. simply disclose sucrose fatty acid ester as a possible lubricant for the composition. Furthermore, the cited reference fails to teach or suggest a specific amount of sucrose fatty acid ester to prevent amorphous cefditoren pivoxil from changing into a crystalline state in a solution, thereby improving the oral absorbability.

Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

Yukiko YOKOI et al.

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